j is 0, 1, or 2;

with the following provisos:

a) where R_2 is C_{1-6} alkyl, Y is other than $-NR_9R_{10}$,

b) where h is 0, het is attached to the a-position via the carbon atom of heterocyclic moiety, and

c) where h is 0, Q is attached to the a-position via the carbon atom of heterocyclic moiety;

and

wherein when Y is –OH and R_1 is substituted phenyl, then R_2 is not C_{1-2} alkyl.—

A marked-up version of amended claim 4 is attached hereto as Attachment A.

REMARKS

Claims 4, 6 and 20-36 are active. Claims 1-3, 5 and 7-19 have been withdrawn from consideration. The Applicants thank Examiner Liu for the courteous and helpful interview of November 21, 2002. Withdrawal of the obviousness rejection was discussed, should no new prior art be found. The Examiner also agreed to reconsider the description rejection of the negative limitations in Claim 4, in view of the description of the excluded subject matter by the specification, and in view of the case law pertaining to the use of provisos in claim language.

The Applicants note support for the prior amendment of the last four lines of Claim 4 in the specification at page 4, lines 8-11 and page 2, line 24-page 3, line 10. Particular R_1 substituents are described at page 8, lines 4-16. Particular R_2 substituents are described at page 8, line 17-page 9, line 20 and page 8, line 20-31. Accordingly, the Applicants do not believe that any new matter has been added.

REJECTION--35 U.S.C. 112, first paragraph

Claims 4 and 20-36 were rejected under 35 U.S.C. 112, first paragraph, as lacking description for the provisos added to Claim 4. These provisos have basis and find support in

the specification at page 4, lines 8-11 and page 2, line 24-page 3, line 10. Particular R_1 substituents are described at page 8, lines 4-16. Particular R_2 substituents are described at page 8, line 17-page 9, line 20 and page 8, line 20-31.

More particularly in the identification of preferred R_2 groups at page 8, line17 – page 9, line 31 of the specification only C_3 and higher alkyl groups are named (see page 8, lines 17-20) hence marking out a clear written description preference for a more limited class wherein R_2 is a C_{3-12} alkyl, i.e., wherein R_2 is not C_{1-2} alkyl. Further a clear preference for Y to be –OH is stated at page 9, line 32. The generic formula of claim 4 is described at page 16, lines 19-23 (Y=-OH) and examples of such compounds are named at page 16, line 25 – page 17, line 33, and all named compounds are ones wherein R_1 is a substituted phenyl and in no named compound is the R_2 group a C_{1-2} alkyl. This provides clear written support for the proviso "wherein when Y is –OH and R_1 is substituted phenyl, then R_2 is not C_{1-2} alkyl." The other two provisos added to claim 4 by amendment have now been deleted as not needed, hence to the extent the rejection of the claims were based upon these two other provisos this amendment moots that basis for rejection.

The Applicants respectfully submit that if the specification adequately describes the larger genus embracing the compounds of Claim 4 and also provides specific description of the particular substituents recited in Claim 4's provisos, then such provisos are adequately described. This is consistent with case law, for instance, In re Johnson and Farnham, 194 USPQ 187 at 196 (CCPA 1977, attached) indicates:

> The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of §112, first paragraph, appears to result from a hypertechnical application of legalistic prose. . .

In the present application, the Applicants have described the broader genus of Claim 4 and have also described the particular substituents recited by the provisos in Claim 4. Thus, consistently with the holding in In re Johnson, the Applicants may decide what bounds of protection they will seek and may retreat to the limited genus described by Claim 4 and its provisos. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

The proviso that remains in claim 4, namely, "wherein when Y is --OH and R_1 is substituted phenyl, then R_2 is not C_{1-2} alkyl" finds written support in the specification. This proviso distinguishes Boyle Chem. Abstract 119:240883 and Freskos Chem. Abstract 129:244921 since each shows the group at the R_2 site to be a methyl group which the proviso excludes. The Griffith Chem. Abstract 108:150945 is distinguished be the original proviso in claim 4 of "a) where R_2 is C_{1-6} alkyl, Y is other than $-NR_9R_{10}$." In the Griffith compound the R_2 site is occupied by a methyl group and the Y site is NH_2 . The a) proviso excludes this combination from the claim.

REJECTION--35 U.S.C. 103

Claims 6 was rejected under 35 U.S.C. 103(a) as being unpatentable over Bender et al., EP 0780386. The Applicants thank Examiner Liu for withdrawing this ground of rejection for independent Claim 4. As discussed in the interview, Bender does not render the compounds of Claim 6 obvious, because this document does not disclose or suggest compounds having a hydroxyl group at the Y position of the present invention.

The rejection does not point out particular compounds in Bender for comparison to the compounds of Claim 6. However, it generally indicates that the compounds of Claim 6 differ from those of Bender, because the substituent at the 2-position of propionic acid is hydroxyl (Y in the present invention) and not hydrogen (R^1 or R^2 of the Bender compound). Substitution of hydrogen in a prior art compound with hydroxyl does not yield a structural isomer or adjacent homolog of the prior art compound, but a structurally different compound.

Moreover, there is no suggestion in Bender to substitute hydroxyl for hydrogen, nor any reasonable expectation in Bender that such a modification of the Bender compound would provide a compound having the utility of that of the present invention. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

The Applicants respectfully submit that this application is now in condition for allowance, in view of the above remarks. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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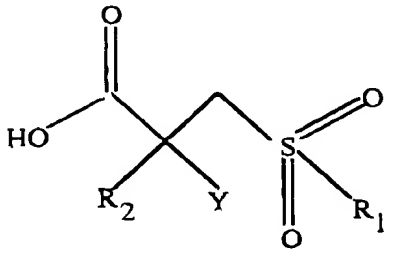
ATTACHMENT A –Marked-up Version

4 (Twice Amended) A compound formula 8:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 is

a) C_{4-12} alkyl,

b) C_{4-12} alkenyl,

c) C_{4-12} alkynyl,

d) $-(CH_2)_h-C_{3-8}$ cycloalkyl,

e) $-(CH_2)_h$-aryl,

f) $-(CH_2)_h$-het,

R_2 is

a) C_{1-12} alkyl,

b) C_{2-12} alkenyl,

c) C_{2-12} alkynyl,

d) $-(CH_2)_h-C_{3-8}$ cycloalkyl,

e) $-(CH_2)_h-C_{3-8}$ cycloalkenyl,

f) $-(CH_2)_h$-aryl,

g) $-(CH_2)_h$-het,

h) $-(CH_2)_h-Q$,

i) $-(CH_2)_i-Q$ or $-(CH_2)_i-RX_4$, optionally the $-(CH_2)_i-$ chain can be substituted with one or two C_{1-4} alkyl or phenyl, which in turn can be substituted with one to three halo or C_{1-4} alkyl, or

l) $-(CH_2)_hCHR_5R_6$;

R_3 is

a) H,

b) C_{3-6} cycloalkyl,

c) C_{1-4} alkyl, or

d) $-(CH_2)_h$-phenyl

X is

a) -O-

b) $-S(=O)_j-$,

c) $-NR_7-$,

d) $-S(=O)_2NR_8-$, or

e) -C(=O)-;

R_4 is

a) H,

b) C_{1-8} alkyl,

c) $-(CH_2)$-phenyl, or

d) $-(CH_2)_h$-het;

R_5 is

a) C_{1-4} alkyl, or

b) $-C(=O)R_3$;

R_6 is

a) $-C(=O)R_3$, or

b) $-(CH_2)_hC(=O)R_3$;

R_7 is

a) H,

b) C_{1-4} alkyl,

c) $-(CH_2)_h$-phenyl,

d) $-C(=O)-R_3$,

e) $-S(=O)_2R_3$, or

f) $-C(=O)_3OR_3$;

R_8 is

a) C_{1-4} alkyl, or

b) $-(CH_2)_h$-phenyl,

Y is

a) -OH,

b) $-NR_9R_{10}$, or

c) fluoro;

R_9 and R_{10} are the same of different and are

a) H,

b) $-C(=O)-R_3$,

c) $-C(=O)-OR_3$, or

d) $-C(=O)-NHR_3$;

aryl is monocarbocyclic, or a bicarbocyclic aromatic moiety;

het is a 5- to 10-membered unsaturated monocyclic or a bicyclic hetrocyclic moiety having one to three atoms selected from the group consisting of oxygen, nitrogen, and sulfur;

Q is a 5- to 10-membered saturated monocyclic or bicyclic heterocyclic moiety having one to two atoms(s) selected from the group consisting of oxygen, nitrogen, and sulfur;

aryl, het, C_{1-12} alkyl, C_{1-4} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, $-C_{3-8}$ cycloalkyl, $-C_{3-8}$ cycloalkenyl, Q and phenyl are optionally substituted;

h is 0, 1, 2, 3, 4, 5, or 6;

i is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

j is 0, 1, or 2;

with the following provisos:

a) where R_2 is C_{1-6} alkyl, Y is other than $-NR_9R_{10}$,

b) where h is 0, het is attached to the a-position via the carbon atom of heterocyclic moiety, and

c) where h is 0, Q is attached to the a-position via the carbon atom of heterocyclic moiety;

[wherein when Y is –OH and R_1 is phenyl substituted with fluorine, then R_2 is not C_{1-2} alkyl,]

[wherein when Y is NH_2 and R_1 is $-CH_2$-phenyl, then R_2 is not C_{1-2} alkyl,] and

wherein when Y is –OH and R_1 is substituted phenyl, then R_2 is not C_{1-2} alkyl.—